Effect of Obicetrapib Across the Spectrum of Background Lipid-Lowering Therapies—Pooled Analyses of the BROADWAY and BROOKLYN Randomised Trials

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Background

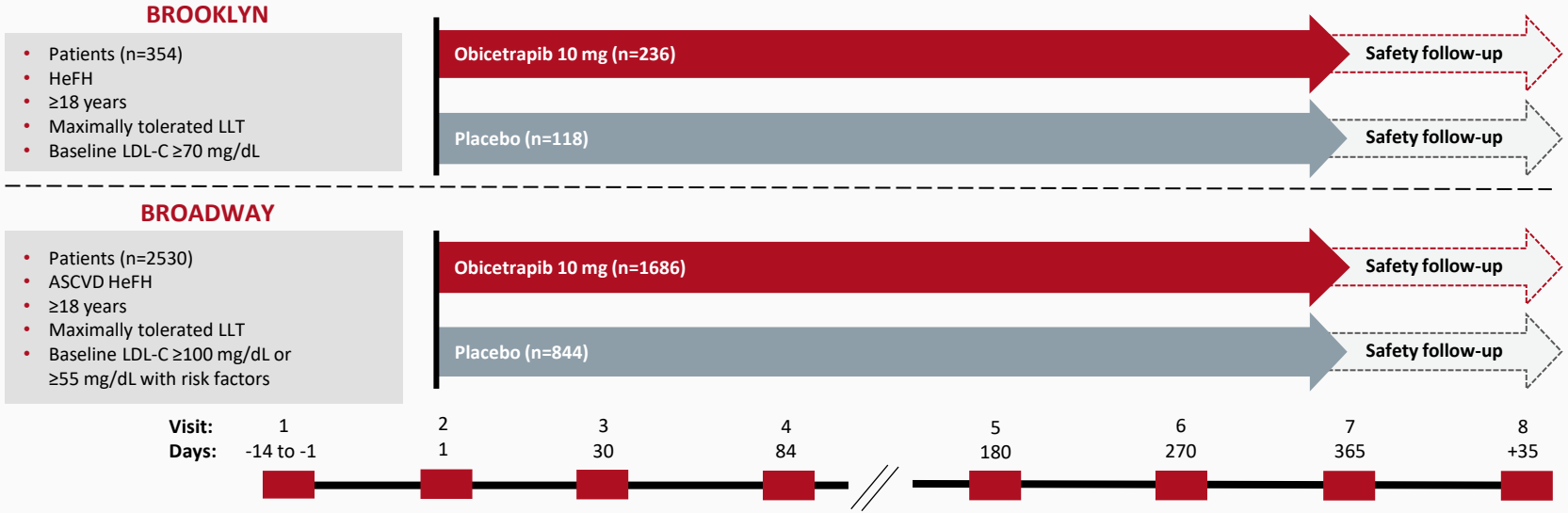
- ESC guidelines recommend more stringent LDL-C goals for patients at very high/high cardiovascular risk[1]
  - Prior ASCVD: LDL-C <55 mg/dL
  - HeFH: LDL-C <70 mg/dL
- Numerous studies have shown that statin monotherapy is insufficient in about 80% of highest cardiovascular risk patients to reach <55mg/dL[2]
  - Need for combination therapy is inevitable for most to achieve risk-based LDL goals
- Obicetrapib **significantly reduced LDL-C** in patients with ASCVD and HeFH in BROADWAY[3] and BROOKLYN[4] trials
- Whether the efficacy of Obicetrapib varies by type and intensity of background LLT is not known[5-9]

ASCVD, atherosclerotic cardiovascular disease; ESC, European Society of Cardiology; HeFH, heterozygous familial hypercholesterolemia; LDL-C, low-density lipoprotein cholesterol; LLT, lipid-lowering therapy.

1. Mach F et al. *Eur Heart J.* 2020;41(1):111-188. **2.** Ray KK et al. *Lancet Reg Health Eur.* 2023;29:100624.**3**. Nicholls SJ et al. *N Engl J Med* 2025;393:51-61**. 4**. Nicholls SJ et al. *Circulation.* 2024;150:e729-e730. **5.** Ballantyne CM et al. *J Clin Lipidol.* 2023;17(4):491-503. **6.** Nicholls SJ et al. *Nat Med.* 2022;28(8):1672-1678. **7.** Dangas K, Navar AM, Kastelein JJP. *Eur Heart J Cardiovasc Pharmacother*. 2022;8(6):622-632. **8.** Kastelein JJP et al. *Curr Atheroscler Rep*. 2024;26(2):35-44. **9.** Ford J et al. *Br J Clin Pharmacol*. 2014;78(3):498-508.

Methods

Pooled analysis of **BROOKLYN** (NCT05425745) and **BROADWAY** (NCT05142722), phase 3, randomized, double-blind, placebo-controlled trials evaluating the effect of Obicetrapib as an adjunct to maximally tolerated LLT



Methods

- Prespecified pooled analysis (n=2778) of BROADWAY and BROOKLYN trials:
  - Randomized participants with ASCVD or HeFH with elevated LDL-C (despite maximally tolerated LLT)
  - 10 mg Obicetrapib once daily or placebo with 1-year follow-up
- Primary endpoint was the placebo-corrected change in LDL from baseline at 84 days
- Secondary endpoints were ApoB and non–HDL-C
- Patients were stratified by binary status (Yes/No) for any statin use, intensity (high, medium, low), ezetimibe, and PCSK9i as well as combination therapy (defined as any 2 classes of medications)

ApoB, apolipoprotein B; HDL-C, high-density lipoprotein cholesterol; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor.

Baseline Characteristics

Parameter	Pooled BROADWAY/BROOKLYN (n=2778)
Select Baseline Characteristics	
Mean Age	64
Female, %	36.1
HeFH, %	26.5
Overall Mean Baseline LDL-C	103 mg/dL
Overall Mean Baseline ApoB	93.4 mg/dL
Overall Mean Baseline non–HDL-C	128 mg/dL
Baseline LLT Use	
High-intensity statin, %	69.3
Moderate-intensity statin, %	21.7
Ezetimibe, %	29.9
PCSK9i, %	5.4
Combination therapy, %	28.3
Monotherapy, %	68.0
No LLT, %	3.6

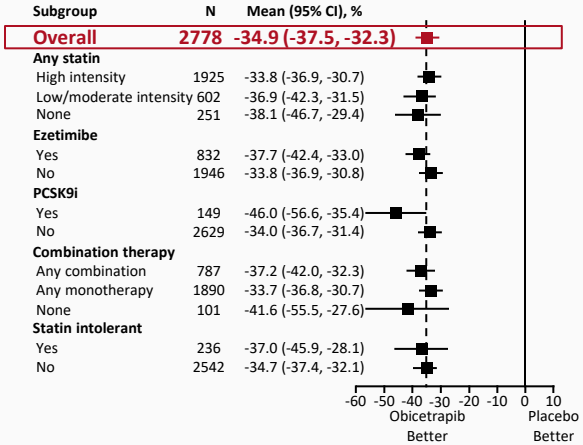
Baseline Lipids Stratified by Baseline LLT*

	Statin			Ezetimibe		PCSK9 Inhibitors		Combination Therapy			Statin Intolerant	
	High	Low/ moderate	None	Y	N	Y	N	Any Combination	Any Monotherapy	None	Y	N
LDL-C, mg/dL	97.0 (37.8)	104.4 (35.4)	144.5 (51.0)	104.0 (39.9)	102.4 (41.4)	113.9 (46.7)	102.2 (40.5)	102.1 (39.5)	99.7 (37.9)	167.8 (53.7)	145.3 (50.8)	98.9 (37.6)
ApoB, mg/dL	90.4 (26.0)	91.9 (24.4)	119.6 (32.5)	96.3 (27.2)	92.1 (27.7)	99.0 (32.0)	93.1 (27.3)	94.8 (26.8)	90.7 (26.0)	132.6 (32.3)	120.1 (32.4)	90.9 (25.7)
Non–HDL-C, mg/dL	121.5 (43.3)	128.3 (40.3)	172.5 (54.4)	128.3 (45.5)	127.3 (46.3)	138.6 (52.1)	126.9 (45.7)	125.9 (44.9)	124.5 (43.0)	196.7 (56.1)	173.2 (54.4)	123.3 (42.9)

*Values are mean (SD).
SD, standard deviation.

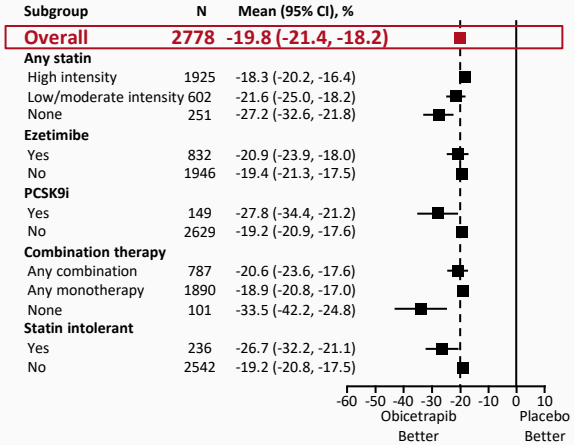
Results

LDL-C

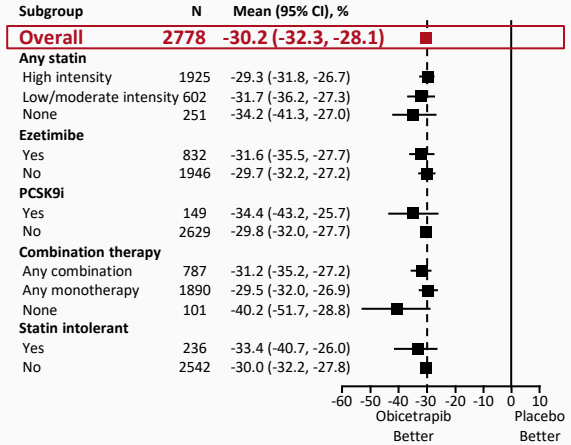


Placebo-corrected reduction in LDL-C with Obicetrapib overall was consistently superior to placebo across the range of background LLT

ApoB



Non–HDL-C



Similar consistent benefits with Obicetrapib as compared with placebo were observed in ApoB and non–HDL-C irrespective of background LLT

CI, confidence interval.

Conclusions

- In very high and high-risk patients with ASCVD or HeFH, Obicetrapib provided significant additional reductions in LDL-C and other atherogenic lipids across the spectrum of concomitant LLTs
- In statin-intolerant patients, Obicetrapib conferred additional benefits of lipoprotein reduction
- Obicetrapib is a promising therapy as an adjunct to existing LLT for patients whose LDL-C remains uncontrolled